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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/681,199	10/09/2003	Juha Kere	0933-0214P	9233

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EXAMINER	
GOLDBERG, JEANINE ANNE	
ART UNIT	PAPER NUMBER
1634	

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
3 MONTHS	04/30/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 04/30/2007.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/681,199	KERE ET AL.	
	Examiner	Art Unit	
	Jeanine A. Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *2/23/07; 4/20/07*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7-9,22,23,25 and 34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7-9,22,23,25 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the papers filed September 25, 2006; February 23, 2007; and April 20, 2007. Currently, claims 1, 7-9, 22-23, 25, 34 are pending.

2. Any objections and rejections not reiterated below are hereby withdrawn.

a. 102(b) rejection over Applied Biosystems Catalog has been withdrawn in view of the amendments to Claim 22 requiring the compound hybridize to SEQ ID NO: 1.

b. The 102(a) rejection over Taipale has been withdrawn in view of the declaration filed on April 20, 2007.

c. The 102(b) rejection over Genbank BE972748 has been withdrawn in view of the amendments to the claims to require a nucleic acid consisting of SEQ ID NO: 1 or the complement of SEQ ID NO: 1.

Maintained Rejections

Priority

3. This application claims priority to 10/364,505, filed February 12, 2003 and provisional application 60/355,782, filed February 12, 2002 and application PCT/FI03/001100, Filed February 12, 2003.

Drawings

4. The drawings are acceptable.

Claim Rejections - 35 USC § 112-Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 22-23, 25, 34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to a kit comprising a compound hybridizing specifically to a nucleic acid sequence of SEQ ID NO: 1.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2b 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed". Applicant is reminded that *Vas-*

Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2b 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...' required a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

The claims are drawn to hybridization language (see Claims 22-23, 25, 34). Example 9 of the written description guidelines states that a structure function relationship with hybridization language may satisfy the written description guidelines. The instant claims do not provide a structure function relationship with hybridization language. Therefore, the hybridization language would encompass sequences from other species, mutated fragment sequences, allelic variants, splice variants, genomic sequences and so forth.

Accordingly, Applicants have not adequately disclosed the relevant identifying characteristics of a representative number of species within the claimed genus.

Response to Arguments

The response traverses the rejection. The response asserts the claims have been amended to overcome the rejection. This argument has been considered but is not convincing because the claim remains drawn to embodiments in which applicants were not in possession of at the time of filing. Specifically, as provided in the Written Description Guidelines, the structure function relationship required for hybridization language has not been presented. Thus for the reasons above and those already of record, the rejection is maintained.

Claim Rejections - 35 USC § 112-Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 22-23, 25, 34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated and purified DYXC1 nucleic acid comprising SEQ ID NO: 1, 13, 15, 17, 19, and the complements thereof, does not reasonably provide enablement for a nucleic acid homolog, variant, fragment or nucleic acid which hybridizes to SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention and breadth of claims

The claims are directed to a kit comprising a compound hybridizing specifically to a nucleic acid sequence of SEQ ID NO: 1.

The invention is in a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The unpredictability of the art and the state of the prior art

The art teaches genetic variations and associations are often irreproducible. Hirschhorn et al. (Genetics in Medicine. Vol. 4, No. 2, pages 45-61, March 2002) teaches that most reported associations are not robust. Of the 166 associations studied three or more times, only 6 have been consistently replicated. Hirschhorn *et al.* suggest a number of reasons for the irreproducibility of studies, suggesting population stratification, linkage disequilibrium, gene-gene or gene-environment interactions, and weak genetic effects and lack of power are possible factors that lead to such irreproducibility. Hirschhorn *et al.* caution that the current irreproducibility of most

association studies should raise a cautionary alarm when considering their use as diagnostics and prognostics (p. 60, Col. 2). Thus, Hirschhorn cautions in drawing conclusions from a single report of an association between a genetic variant and disease susceptibility.

Additionally, Ioannidis (Nature Genetics, Vol. 29, pages 306-309, November 2001) teaches that the results of the first study correlate only modestly with subsequent research on the same association (abstract). Ioannidis teaches that both bias and genuine population diversity might explain why early association studies tend to overestimate the disease protection or predisposition conferred by a genetic polymorphism (abstract).

The art teaches that presence of SNPs in the same gene does not indicate that each of the genes is associated with the same diseases. Meyer et al. (PG Pub 2003/0092019), for example, teaches that SNPs in the CADPKL gene are not each associated with neuropsychiatric disorders such as schizophrenia. Specifically Meyer teaches that cadpkl5 and cadpkl6 are not associated with the disease, however cadpkl7 has a p-value of less than 0.05, therefore an association exists. Each of these polymorphisms are SNPs within the CADPKL gene, however, it is apparent that they are not all associated in the same manner with disease. Thus, Meyer exemplifies that the association of a single SNP in a gene does not indicate that all SNPs within the gene are associated with the disease.

The art teaches a family-based association study that does not support DYX1C1 on 15q21.3 as a candidate gene in developmental dyslexia. Marino et al. (E. J. Human Genetics, Vol. 13, pages 491-499, 2005) teaches 8 SNPs, three of which were suitable for genetic analysis. The analyses did not support the involvement of the DYX1C1 gene variants in this sample of dyslexics and their relatives. Marino states that "we were

unable to replicate the original findings between DYX1C1 gene and developmental dyslexia, perhaps due to genetic heterogeneity. Mario states that haplotype analysis further increased the number of informative families (page 498, col. 1).

Scerri et al. (J. Med. Genet. Vol. 41, pages 853-857, 2004) teaches putative functional alleles of DYX1C1 are not associated with dyslexia susceptibility in a large sample of sibling pairs from the UK. Scerri teaches that only one of eight sequence variants showed nominally any significant association with any of the quantitative measures. Scerri teaches that the DYX1C1 alleles previously associated with dyslexia are not associated with the trait in their sample. Scerri teaches that, like Wigg, the data of their study, that a biased transmission of the –3G/1249G haplotype children with poorer reading related skills (opposite finding to the original report by Taipale) (page 857, col. 1).

Wigg et al (Mol. Psychiatry, Vol. 9, pages 1111-1121, 2004) teaches support for EKN1 as the susceptibility locus for dyslexia on 15q21. Wigg teaches that EKN1, with unknown function in the linked region was identified via a translocation breakpoint. Wigg analyses several polymorphisms, however, only the 1249 polymorphism appears to be individually associated with dyslexia. Wigg further teaches haplotype analysis and that haplotype analysis increases the power of the analysis (page 1117, col. 2). Wigg teaches that the relevant DNA changes may be located in regulatory sequences, and the regions that must be screened may be quite large given that these regions have not been yet delineated (page 1120, col. 2). Further Wigg acknowledges that these are preliminary findings and further replication studies are necessary before definitive conclusions can be made (col. 1120, col. 2).

Guidance in the Specification and Working Examples

The specification teaches a DYXC1 nucleic acid sequence for human (SEQ ID NO: 1); mouse (SEQ ID NO: 4), pan troglodytes (SEQ ID NO: 13), gorilla (SEQ ID NO: 15), Pongo pygmaeus (SEQ ID NO: 17) and Pan paniscus (SEQ ID NO: 19). Further, the specification teaches 8 polymorphisms within DYXC1 nucleic acid of SEQ ID NO: 1. Table 1 illustrates the frequency of single nucleotide polymorphisms in dyslexic subjects and controls. Only two polymorphisms appear to show any association with dyslexia at a significant level. –3G to A and 1249 G-T. The guidance provided by the specification amounts to an invitation for the skilled artisan to try and follow the disclosed instructions to make and use the claimed invention.

Quantity of Experimentation

The quantity of experimentation in this area is extremely large since there is significant number of parameters which would have to be studied before the skilled artisan would be able to used the claimed invention as broadly as claimed.

While nucleic acids which may hybridize to the DYXC1 may be obtained through hybridization analysis. The skilled artisan would be unable to use these variant nucleic acids without further unpredictable and undue experimentation.

Given the lack of teachings in the art and the specification regarding the function of DYXC1, it is unclear how the skilled artisan would know they have obtained a DYXC1 homolog of a dog or cat nucleic acid, for example. The specification fails to provide any function for the claimed nucleic acid homologs. Further, the wide range of similarity between primates, for example, would not allow the skilled artisan to immediately recognize the presence of a DYXC1 nucleic acid.

With respect to variants of DYXC1, both the specification and the post-filing date art support that not all SNPs or variants are associated with dyslexia. The skilled

artisan would not be appraised of how to use variant nucleic acids which are not associated with dyslexia. As seen in Table 1, -164; -2; 4; 271; 572; 1259 do not have a significant association with dyslexia. Similarly, the post filing date art supports that these polymorphisms and additional polymorphisms are not associated in a significant manner with dyslexia.

To use the claimed invention to the full scope of the instant claims would require years of inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

In the instant case, as discussed above, in a highly unpredictable art for determining the function of newly identified nucleic acids, for the skilled artisan to be able to practice the claimed invention as broadly as claimed, the skilled artisan would be required to perform additional and undue and unpredictable experimentation. Further, the prior art and the specification provides insufficient guidance to overcome the art recognized difficulties in assigning function to particular nucleic acids. Obtaining nucleic acids which hybridize to particular nucleic acids would be routine in the art, however, assigning the nucleic acids as DYXC1 nucleic acids or having a particular function that would enable the skilled artisan to use the nucleic acids would have been undue and unpredictable at the time the invention was made. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of

guidance provided in the specification, the absence of a working example and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Response to Arguments

The response traverses the rejection. The response asserts the claims have been amended to overcome the rejection. This argument has been considered but is not convincing because the claim remains drawn to embodiments in which applicants had not enabled at the time of filing. As discussed in the rejection above, the skilled artisan would not know how to use any nucleic acid which hybridizes with SEQ ID NO: 1. As provided in the specification numerous allelic variations do not appear to be associated or linked to dyslexia. Therefore, it is undue experimentation to determine how the skilled artisan would use the claimed invention. Thus for the reasons above and those already of record, the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 22-23, 25, 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brennan (US Patent 5,474,796, December 12, 1995) in view of Ahern (The Scientist, Vol 9, No. 15, page 20, July 1995).

Brennan teaches oligonucleotides having 10 nucleotides each (10-mers). The oligonucleotides represent every possible permutation of the 10-mer oligonucleotide.

Brennan does not specifically teach placing the array with instructions into a kit.

However, Ahern teaches reagent kits offer scientists good return on investment. Ahern teaches kits save time and money because the kits already comes prepared.

Therefore, it would have been **prima facie** obvious to one of ordinary skill in the art at the time the invention was made to have modified the teachings of Brennan with the teachings of Ahern to incorporate the necessary reagents into a packaged kit. The ordinary artisan would have been motivated to have packaged the primers, probes, and reagents of Brennan into a kit, as taught by Ahern for the express purpose of saving time and money.

With regard to the limitation that the kits contain instructions, the inclusion of instructions is not considered to provide a patentable limitation on the claims because the instructions merely represent a statement of intended use in the form of instructions in a kit. See In re Ngai, 367 F.3d 1336, 70 U.S.P.Q.2d 1862 (Fed. Cir. 2004)(holding

that an inventor could not patent known kits by simply attaching new set of instructions to that product).

Response to Arguments

The response traverses the rejection. The response asserts Brennan teaches a particular structure, a compound that specifically hybridizes to a nucleic acid sequence of SEQ ID NO: 1." This argument has been reviewed but is not persuasive because the 10-mers of Brennan would hybridize specifically with the nucleic acid sequence of SEQ ID NO: 1. Thus for the reasons above and those already of record, the rejection is maintained.

Conclusion

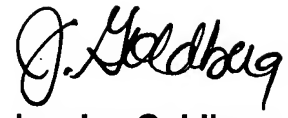
9. No claims allowable.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (571) 272-0743. The examiner can normally be reached Monday-Friday from 7:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The Central Fax Number for official correspondence is (571) 273-8300.



Jeanine Goldberg
Primary Examiner
April 23, 2007